



3

8-2-04

1615 \$  
if

Docket No. 57273 (47126)

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: G. Cevc Confirmation No.: 9461  
U.S.S.N.: 09/555,986 Group No.: 1615  
FILED: August 17, 2000 Examiner: G.S. Kishore  
FOR: METHOD FOR DEVELOPING, TESTING AND USING ASSOCIATES  
OF MACROMOLECULES AND COMPLEX AGGREGATES FOR  
IMPROVED PAYLOAD AND CONTROLLABLE DE/ASSOCIATION  
RATES

08/04/2004 NROCHA1 00000000 09555986

Mail Stop: Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 02209-9169

01 FC:1806

180.00 OP

\*\*\*\*\*

CERTIFICATE OF EXPRESS MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as Express Mail, Label No. EV 437 825 112 US addressed to the: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Date: July 30, 2004

By:

Judy Daley

\*\*\*\*\*

Sir:

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

In accordance with the provisions of 37 C.F.R. §§1.56 and 1.97, Applicants herewith submit the publications and/or patents shown on the attached form PTO-1449, for consideration by the Examiner in connection with the examination of the above-identified patent application.

**REMARKS**

In accordance with the provisions of 37 C.F.R. §1.97, this statement is being filed:

- (1) within three (3) months of the Filing Date or **before the mailing date of the First Office Action** on the merits; or

- \_\_\_\_\_ (2) within three months of the mailing date of the Search Report issued by the PCT Patent Office; or
- \_\_\_\_\_ (3) after the period defined in (1) but before the mailing date of a **Final Rejection** or **Notice of Allowance**, and the requisite Certification or fee under Rule 1.17(p), namely **\$180.00**, is included herein; or
- X   (4) after the mailing date of a **Final Rejection** or **Notice of Allowance** but before the payment of the **Issue Fee**, and the requisite Certification, petition, and petition fee are included herein.

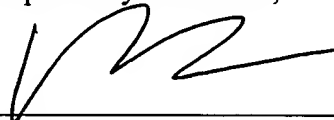
It is respectfully requested that each of the documents shown on the attached form(s) PTO-1449 be made of record in this application. Copies of these documents (CHECK ONE):

- X   are enclosed herewith; or
- \_\_\_\_\_ have been cited in the parent application, and are thus not being resubmitted herein.

#### FEE AUTHORIZATION

Enclosed herewith is a check in the amount of \$180.00 for submission of these cited references. Should any additional fees associated with the submission be required, the Commissioner is authorized to charge the missing fee to our Deposit Account, No. 04-1105. Any overpayments should be credited to said Deposit Account.

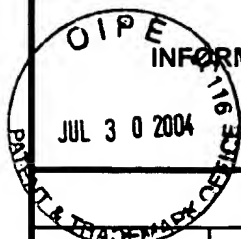
Respectfully submitted,



Date: July 30, 2004

\_\_\_\_\_  
Peter F. Corless (Reg. No. 33,860)  
Edwards & Angell, LLP  
P.O. Box 55874  
Boston, MA 02205  
(617) 439-4444

Customer No.: 21874

**INFORMATION DISCLOSURE CITATION**

(Use several sheets if necessary)

ATTY DOCKET NO.

57273 (47126)

SERIAL NO.

09/555,986

Applicant(s): G. CEVC

FILING

August 17, 2000

GROUP

1615

**U.S. PATENT DOCUMENTS**

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	AA	5,607,692	04/04/1997	Ribier et al.	424	450	
	AB	5,958,379	28/09/1999	Regenold et al.	424	47	
	AC	4,911,928	27/03/1990	Wallach	424	450	
	AD	5,322,685	21/06/1994	Nakagawa et al.	424	78.03	
	AE	5,238,613	24/08/1993	Anderson	264	22	
	AF	Re. 33,273	24/07/1990	Speaker	210	639	
	AG	4,619,794	28/10/1986	Hauser	264	4.1	
	AH	4,954,345	04/09/1990	Müller	424	450	
	AI	4,937,078	26/06/1990	Mezei et al.	424	450	
	AJ	4,921,706	01/05/1990	Roberts et al.	424	450	
	AK	5,741,515	21/04/1998	Ciceri et al.	424	450	

**FOREIGN PATENT DOCUMENTS**

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	BA	07-324029	12.12.1995	JP				
	BB	0 393 707	20.04.1990	CA				
	BC	1 143 656	20.04.1990	CA				

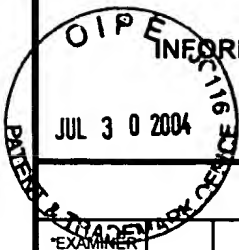
**OTHER DOCUMENTS** (Including Author, Title, Date, Pertinent Pages, Etc.)

	CA	G. Cevc et al., Transdermal drug carriers: basic properties, optimization and transfer efficiency in the case of epicutaneously applied peptides, <i>J. Contr. Rel.</i> , 36, pp. 3-16, 1995
	CB	S. Yuan, et al., Cationic Liposome and Gene Transfer, <i>Progress in Physiological Science</i> , 28(2), pp. 163-165, 1997

EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**INFORMATION DISCLOSURE CITATION***(Use several sheets if necessary)*

ATTY DOCKET NO.

57273 (47126)

SERIAL NO.

09/555,986

Applicant(s): G. CEVC

FILING

August 17, 2000

GROUP

1615

**U.S. PATENT DOCUMENTS**

*EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

**FOREIGN PATENT DOCUMENTS**

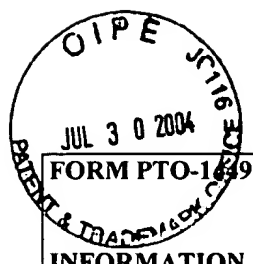
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	BD	61-271204	01.12.1986	JP				
	BE	724218	17.10.1996	AU				
	BF	0 152 379	11.02.85	EP				
	BG	0 088 046	11.02.1983	EP				

**OTHER DOCUMENTS** *(Including Author, Title, Date, Pertinent Pages, Etc.)*


EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



FORM PTO-1629

<b>DOCKET NO:</b> 57273 (47126)	<b>SERIAL NO.:</b> 09/555,986
<b>APPLICANT:</b> G. CEVC	
<b>FILING DATE:</b> August 17, 2000	<b>GROUP NO.</b> 1615

**INFORMATION DISCLOSURE STATEMENT**

**UNITED STATES PATENT DOCUMENTS**

EXAM. INITIALS		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

**FOREIGN PATENT DOCUMENTS**

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO
	BH	WO 98/30215	16.07.1998	PCT			
	BI	WO 88/07362	06.10.1988	PCT			
	BJ	WO 98/06750	19.02.1998	PCT			
	BK	WO 91/04013	04.04.1991	PCT			
	BL	WO 92/05771	16.04.1992	PCT			
	BM	WO 93/19736	14.10.1993	PCT			
	BN	WO 93/19737	14.10.1993	PCT			

<b>EXAMINER:</b>	<b>DATE:</b>
------------------	--------------



<b>FORM PTO-1449</b>			<b>DOCKET NO:</b> 57273 (47126)		<b>SERIAL NO.:</b> 09/555,986		
<b>INFORMATION DISCLOSURE STATEMENT</b>			<b>APPLICANT: G. CEVC</b>				
			<b>FILING DATE:</b> August 17, 2000		<b>GROUP NO.</b> 1615		
<b>UNITED STATES PATENT DOCUMENTS</b>							
<b>EXAM. INITIALS</b>		<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>NAME</b>	<b>CLASS</b>	<b>SUBCLASS</b>	<b>FILING DATE IF APPROPRIATE</b>
<b>FOREIGN PATENT DOCUMENTS</b>							
		<b>DOCUMENT NUMBER</b>	<b>DATE</b>	<b>COUNTRY</b>	<b>CLASS</b>	<b>SUBCLASS</b>	<b>TRANSLATION YES/NO</b>
	BO	WO 90/09782	07.09.1990	PCT			
	BP	WO 87/01938	09.04.1987	PCT			
	BQ	4,447,287	07.11.1996	DE			
	BR	3,713,494	29.10.1987	DE			
	BS	3,016,976	13.11.1980	DE			
	BT	1,289,420	24.09.1991	CA			
	BU	1,740,283	28.07.1983	AU			
	BV	0,674,913	04.10.1995	EP			
	BW	0,704,206	03.04.1996	EP			
	BX	0,475,160	18.03.1992	EP			
	BY	0,707,847	24.04.1996	EP			
	BZ	0,280,492	31.08.1988	EP			
	BAA	0,102,324	07.03.1984	EP			
	BBB	0,224,837	24.11.1986	EP			
	BCC	0,211,647	25.02.1987	EP			
	BDD	0,220,797	06.05.1987	EP			
<b>EXAMINER:</b>					<b>DATE:</b>		



## INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Docket Number (Optional)

57273 (47126)

Application Number

09/555,986

Applicant(s)

G. CEVC

Filing Date

August 17, 2000

Group Art Unit

1615

\*EXAMINER

INITIAL

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

CC

G. Cevc, Transfersomes, Liposomes and Other Lipid Suspensions on the Skin: Permeation Enhancement, Vesicle Penetration, and Transdermal Drug Delivery, *Crit. Rev. Ther. Drug Carrier Syst.*, 13(3&4), pp. 257-388, 1996

CD

T. Henmi, et al., "Application of an Oily Gel Formed by Hydrogenated Soybean Phospholipids as a Percutaneous Absorption-Type Ointment Base," *Chem. Pharm. Bull.*, 42(3), pp. 651-655, 1994

CE

Benner, "The Human Body, The Wonderwork of the Human Body, Structure, Functions, Interactions, Processes and Mechanisms," Weltbild GmbH Augsburg (1995)

CF

Serva, FEINBIOCHEMICA FUR FORSCHUNG for *Serva Feinbiochemica GmbH & Co.* (1986/1987)

CG

Clark, J.M., Jr., "Experimental Biochemistry" Biochemistry Division, Department of Chemistry, University of Illinois, pp. 47-48

CH

Patel, H.M., "Liposomes as a Controlled-release System" Biomedical Society Transactions 609th Meeting, Leeds, pp.513-516

CI

Fieser, L.F., et al. "Organische Chemie" *Hans Ruprecht Hensel, 2nd revised edition, Verlag Chemie GmbH, Weinheim/Bergstr* (1968)

CJ

Fluka Chemika-BioChemika Catalogue 16 (1988/89)

CK

Roeding, J., "Liposomes and Niosomes in Pharmacy and Cosmetic State of the Art Prospects, Techniques of Visualizing Vesicular Systems, Interaction of Liposomes with the Skin" *Training Course No. 105 from May 14 to 16, 1990, MARITIM Hotel Nurnberg, Frauentorgraben 11, 8500 Nurenberg*

CL

L. Lobbbecke, et al., "Effects of Short-Chain Alcohols On the Phase Behavior And Interdigitation Of Phosphatidylcholine Bilayer Membranes," *Biochimica et Biophysica Acta*, 1237, pp. 59-69, 1995

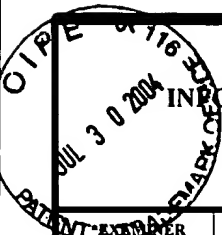
CM

R. Singh, et al., "Liposomally Encapsulated Diclofenac For Sonophoresis Induced Systemic Delivery," *J. Microencapsulation*, Vol. 12, No. 2, pp. 149-154, 1995

EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP Section 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



## INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Docket Number (Optional)

57273 (47126)

Application Number

09/555,986

Applicant(s)

G. CEVC

Filing Date

August 17, 2000

Group Art Unit

1615

EXAMINER  
INITIAL

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

CN

M. Foldvari, et al., "Dermal Drug Delivery by Liposome Encapsulation: Clinical and Electron Microscopic Studies," *J. Microencapsulation*, Vol. 7, No. 4, pp. 479-489, 1990

CO

M. Foldari, "In Vitro cutaneous and Percutaneous Delivery and in Vivo Efficacy of Tetracaine from Liposomal and Conventional Vehicles," *Pharmaceutical Research*, Vol. 11, No. 11, 1994

CP

M. Foldari, "Effect of Vehicle on Topical Liposomal Drug Delivery: Petrolatum Bases," *J. Microencapsulation*, Vol. 13, No. 5, pp. 589-600, 1996

CQ

M.E. Planas, et al., "Noninvasive Percutaneous Induction of Topical Analgesia by a New Type of Drug Carrier, and Prolongation of Local Pain Insensitivity by Anesthetic Liposomes," *Anesth. Analg.*, 75, pp. 615-621, 1992

CR

H. Peters, et al., "Pharmacodynamics of a Liposomal Preparation for Local Anaesthesia," *Arzneim.-Forsch./Drug Res.*, 45(II), Nr. 12, 1995

CS

I. Stoye, et al., "Transformation of a Liposomal Dispersion Containing Ibuprofen Lysinate and Phospholipids into Mixed Micelles - Physico-chemical Characterization and Influence on Drug Permeation through Excised Human Stratum Corneum," *European Journal of Pharmaceutics and Biopharmaceutics*, 46, pp. 191-200, 1998

CT

J. Schramlova, et al., "The Effect of an Antiphlogistic Incorporated in Liposomes on Experimentally Induced Inflammation," *Folia Biologica (Praha)*, 43, pp. 195-199, 1997

CU

G. Cevc, "Drug Delivery Across the Skin," *Exp. Opin. Invest. Drugs*, 6(12), pp. 1887-1937, 1997

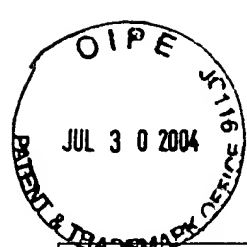
EXAMINER

DATE CONSIDERED

\*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP Section 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.



FORM PTO-1449		DOCKET NO: 57273 (47126)		SERIAL NO.: 09/555,986			
INFORMATION DISCLOSURE STATEMENT		APPLICANT: G. CEVC					
		FILING DATE: August 17, 2000		GROUP NO. 1615			
UNITED STATES PATENT DOCUMENTS							
EXAM. INITIALS		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO
OTHER DOCUMENTS							
	CV	G. CEVC et al., Transfersomes-mediated transepidermal delivery improves the regio-specificity and biological activity of corticosteroids in vivo, <i>Journal of Controlled Release</i> 45 (1997) 211-226					
	CW	V.M. KNEPP et al., CONTROLLED DRUG RELEASE FROM A NOVEL LIPOSOMAL DELIVERY SYSTEM II. TRANSDERMAL DELIVERY CHARACTERISTICS," <i>Journal of Controlled Release</i> , 12 (1990) March, No. 1, Amsterdam, NL, pp. 25-30					
	CX	C.E. Price, "A REVIEW OF THE FACTORS INFLUENCING THE PENETRATION OF PESTICIDES THROUGH PLANT LEAVES" on I.C.I. Ltd., Plant Protection Division, Jealott's Hill Research Station, Bracknell, Berkshire RG12 6EY, U.K., pp. 237-252					
	CY	K. Karzel and R. K. Liedtke, "MECHANISMEN TRANSKUTANER RESORPTION" on Grandlagen/Basics, pp. 1487-1491					
	CZ	Michael Mezei, "LIPOSOMES AS A SKIN DRUG DELIVERY SYSTEM" 1985 Elsevier Science Publishers B.V. (Biomedical Division), pp. 345-358					
	CAA	Adrienn Gesztes and Michael Mezei, "TOPICAL ANESTHESIA OF THE SKIN BY LIPOSOME-ENCAPSULATED TETRACAINE" on <i>Anesth Analg</i> 1988; 67: pp. 1079-81					
	CBB	A. Helenius, et al, "SOLUBILIZATION OF MEMBRANES BY DETERGENTS," <i>Biochimica et Biophysica Acta</i> , 415 (1975) 29-79					
	CCC	Phillip G. Green, et al., "IN VITRO AND IN VIVO ENHANCEMENT OF SKIN PERMEATION WITH OLEIC AND LAURIC ACIDS" on <i>International Journal of Pharmaceutics</i> , 48 (1988), pp. 103-111					
	CDD	Guia M. Golden et al., "ROLE OF STRATUM CORNEUM LIPID FLUIDITY IN TRANSDERMAL DRUG FLUX" on <i>Journal of Pharmaceutical Sciences</i> , Vol. 76, No. 1, January 1987, American Pharmaceutical Association, pp. 25-28					
	CEE	Bruce J. Aungst et al., "ENHANCEMENT OF NALOXONE PENETRATION THROUGH HUMAN SKIN IN VITRO USING FATTY ACIDS, FATTY ALCOHOLS, SURFACTANTS, SULFOXIDES AND AMIDES" on <i>International Journal of Pharmaceutics</i> , 33 (1986) pp. 225-234					



FORM PTO-1449		DOCKET NO: 57273 (47126)		SERIAL NO.: 09/555,986			
INFORMATION DISCLOSURE STATEMENT		APPLICANT: G. CEVC					
		FILING DATE: August 17, 2000		GROUP NO. 1615			
UNITED STATES PATENT DOCUMENTS							
EXAM. INITIALS		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO
OTHER DOCUMENTS							
	CFF	Ronald R. Burnette et al., "CHARACTERIZATION OF THE PERMSELECTIVE PROPERTIES OF EXCISED HUMAN SKIN DURING LONTOPHORESIS" on <i>Journal of Pharmaceutical Sciences</i> , Vol. 76, No. 10, October 1987, American Pharmaceutical Association, pp. 765-773					
	CGG	E.C. Katoulis et al., "EFFICACY OF A NEW NEEDLELESS INSULIN DELIVERY SYSTEM MONITORING OF BLOOD GLUCOSE FLUCTUATIONS AND FREE INSULIN LEVELS" on <i>International Journal of Artificial Organs</i> , Vol. 12, No. 5, 1989, pp. 333-338					
	CHH	Ovals Siddiqui et al., "NONPARENTAL ADMINISTRATION OF PEPTIDE AND PROTEIN DRUGS" on <i>CRC Critical Reviews in Therapeutic Drug Carrier Systems</i> , Volume 3, Issue 3, pp. 195-208					
	CII	Cevc, G. et al., "Ultraflexible vesicles, Transfersomes, have an extremely low pore penetration resistance and transport therapeutic amounts of insulin across the intact mammalian skin," <i>Biochimica et Biophysica Acta</i> . 1368 pp. 201-215 (1998)					
	CJJ	Cevc, G., "Material Transport Across Permeability Barriers by Means of Lipid Vesicles," <i>Handbook of Biological Physics</i> , Vol. 1, pp. 465-490 (1995)					
	CKK	Mayer, L.D. et al., "Vesicles of variables sizes produced by a rapid extrusion procedure," <i>Biochimica et Biophysica Acta</i> , 858 pp. 161-165 (1986)					
	CLL	Patel, H.M. et al., "ORAL ADMINISTRATION OF INSULIN BY ENCAPSULATION WITHIN LIPOSOMES," <i>FEBS LETTERS</i> , 62(1):60-63 (February 1976)					
	CMM	Schreier, H., "Liposomes – A Novel Drug Carrier, I. Phospholipids; Production and Characterization of Liposomes; II. Destiny of liposomes in vivo; use in therapy," <i>Pharmazie in unserer Zeit</i> , No. 4 (1982)					
	CNN	Beyer, C. et al., "Micro Emulsions" <i>Pharmazie in unserer Zeit</i> , No. 2 (1983)					
	COO	Lichtenberg, D. et al., "SOLUBILIZATION OF PHOSPHOLIPIDS BY DETERGENTS STRUCTURAL AND KINETIC ASPECTS" <i>Biochimica et Biophysica Acta</i> , 737 pp. 285-304 (1983)					
EXAMINER:							



FORM PTO-1449		DOCKET NO: 57273 (47126)		SERIAL NO.: 09/555,986			
INFORMATION DISCLOSURE STATEMENT		APPLICANT: G. CEVC					
		FILING DATE: August 17, 2000		GROUP NO. 1615			
UNITED STATES PATENT DOCUMENTS							
EXAM. INITIALS		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS							
		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES/NO
OTHER DOCUMENTS							
	CPP	Lasch, J. et al., "Interactions of external lipids (lipids vesicles) with the skin" <i>Journal of Liposome Research</i> , 5(3) pp. 543-569 (1995)					
	CQQ	Berger, M., "Oral Insulin 1922-1992: The History of Continuous Ambition and Failure" Heinrich-Heine-University, Dusseldorf, Germany					
	CRR	Cevc. G. et al., "The skin: a pathway for systemic treatment with patches and lipid-based agent carriers" <i>Advanced Drug Delivery Reviews</i> 18 pp. 349-378 (1996)					
	CSS	M.L. Jackson, et al., "SOLUBILIZATION OF PHOSPHATIDYLCHOLINE BILAYERS BY OCTYL GLUCOSIDE," <i>biochemistry</i> , 1982, 21, 4576-4582					
	CTT	P. Vinson, et al., "VESICLE-MICELLE TRANSITION OF PHOSPHATIDYLCHOLINE AND OCTYL GLUCOSIDE ELUCIDATED BY CRYO-TRANSMISSION ELE TRON MICROSCOPY," <i>Biophys. J., Biophysical Society</i> , Volume 56 October 1989 669-681					
	CUU	K. Edwards, et al., "EFFECTS OF TRITON X-100 ON SONICATED LECITHIN VESICLES," <i>Langmuir</i> , Vol. 5, No. 2, 1989 pp. 473-478					
	CVV	A. Brendzel, et al., "EFFECTS OF LIPID-SOLUBLE SUBSTANCES ON THE THERMOTROPIC PROPERTIES OF LIPOSOME FILTRATION," <i>Biochimica et Biophysica Acta</i> , 601 (1980) 260-270					
	CWW	G. Blume, et al., "DRUG-CARRIER AND STABILITY PROPERTIES OF THE LONG-LIVED LIPID VESICLES, CRYPTOSOMES, IN VITRO AND IN VIVO," <i>Journal of Liposome Research</i> , 2(3), 355-368 (1992)					
EXAMINER:					DATE:		